

Acute hemorrhagic edema of infancy after MMR vaccine

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Acute hemorrhagic edema of infancy (AHEI) is a rare type of leukocytoclastic vasculitis. It affects mainly children less than two years of age. Many precipitating factors have been reported, including infectious etiology and vaccination. We are reporting a two-year-old boy with AHEI after measles, mumps, and rubella (MMR) vaccine. To our knowledge this is the second reported case after an MMR vaccine.

Acute hemorrhagic edema of infancy (AHEI) is a rare type of cutaneous vasculitis. Despite its impressive clinical presentation, it has a very benign course limited to skin and resolves in three weeks. Trigger factors have been reported including drugs, infections and vaccination. Measles, mumps, and rubella (MMR) vaccine has been implicated once before as a precipitating factor by Blasini et al.¹

CASE

A two-year-old male presented to our clinic with a 5-day history of progressive dusky red indurated plaques with a targetoid appearance over the extremities and face. The ears and cheeks were swollen and edematous (**Figure 1**). There was no history of preceding infection or medication intake. However, he was vaccinated for MMR two weeks before presentation. He had no systemic symptoms. A skin biopsy showed leukocytoclastic vasculitis, with fibrinoid necrosis of the blood vessels, extravasation of RBCs, karyorrhexis and neutrophilic infiltrates (**Figure 2**). However, direct immunofluorescence was not done. Blood tests were normal including CBC, kidney and liver function test and ESR, but CRP was 17.5 mg/L. Mycoplasma and herpes simplex virus type 1 and 2 serology tests were all negative. He was labeled as AHEI based on clinical presentation and the skin biopsy. He was given a short course of prednisolone 1 mg/kg (12 mg) over three weeks. On follow up one month later, the lesions cleared completely.

DISCUSSION

AHEI is a rare small-vessel leukocytoclastic vasculitis. Snow et al² described the first case in the United States in 1913, but the description of the disease in Europe only appeared in 1938 by Finkelstein³ and later by Seidlmayer as “Seidlmayer cockade purpura”.⁴ More than 80% of cases have been reported in children less



Figure 1. Dusky red targetoid edematous plaques over face and arm.

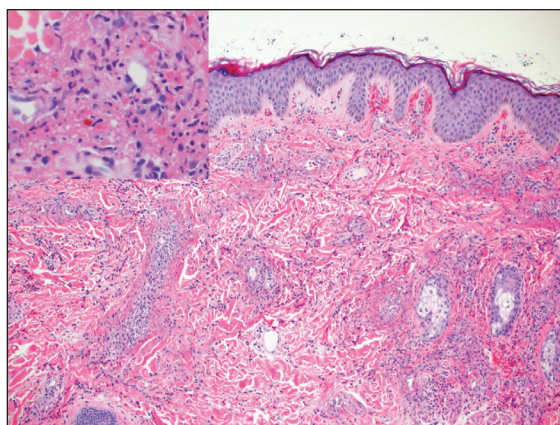


Figure 2. Skin biopsy showing leukocytoclastic vasculitis.

than two years of age, but it has been reported in children at five years of age and the male to female ratio is 2:1.1,⁵ In addition, a congenital case was reported after maternal gastroenteritis six weeks before delivery.⁶ It occurs more during winter, which supports infectious agents as a triggering factor.⁷

Children with AHEI usually have fever, nonpitting edema and indurated dusky red plaques with a targetoid or annular purpuric configuration. It affects the face and ears, sparing the trunk in most cases. However, severe truncal involvement has been reported as well.^{5,8,9} The edema occurs mainly over the face and ears,^{5,10,11} and is associated typically with a low grade fever in 50% of cases. Despite the dramatic presentation the child looks well and nontoxic. A rare bullous variant was reported in a 9-month-old child.¹² Other uncommon presentations are pruritus, urticaria, conjunctival injection and oral petechiae.¹⁰

Despite the dramatic presentation, most of blood tests are normal. The erythrocyte sedimentation rate and C-reactive protein can be elevated. Skin biopsy shows fibrinoid necrosis, extravasation of red blood cells, leukocytoclasia. 10% of these patients will have perivascular IgA deposition detected by direct immunofluorescence.

AHEI generally has a benign course with aduration of illness lasting 1 to 3 weeks.^{5,10,11} However, very

rare complications have been reported including intussusception,⁷ hematuria, proteinuria, hypocomplementemia¹³ and scarring.¹⁴ Other systemic symptoms such as abdominal pain, gastrointestinal bleeding, arthritis and nephritis have been rarely reported as well.¹⁵ Severe articular involvement has been described in one case¹⁶ as well as testicular torsion.¹⁰ Mucosal involvement is rare.^{17,18}

The differential diagnosis of AHEI includes Henoch-Schönlein purpura (HSP), meningococemia, erythema multiforme, Kawasaki disease, and drug eruption.

The distinction between AHEI and HSP is among the most challenging. HSP usually affects children between 2-10 years with predominant lower limb involvement and minimal edema. HSP commonly has systemic involvement with a 50% chance of recurrence. On direct immunofluorescence, IgA deposition is noted in most cases with HSP.^{5,10-12,19,20}

Many triggers have been reported. However, no strong evidence suggest one more than the other. Among them are infections, drugs and vaccination. The average interval between the onset of AHEI and the possible causative agent ranges from two days to one month.^{5,10,11} AHEI was reported after vaccination with *Bacillus Calmette-Guérin* (BCG) 11, H1N1,^{19,21} Hemophilus influenza type B, diphtheria, tetanus, acellular pertussis, hepatitis B, polio, and conjugate pneumococcal vaccines.²² Blasini et al¹ reported a 12-month-old male who presented with a two-day history of a purple rash and swelling on the legs, palms, soles, and earlobes. He had a 10-day history of upper respiratory infection, fever, conjunctivitis, and vomiting treated with tobramycin, amoxicillin, and ibuprofen. Approximately three weeks prior to admission, he received vaccines for varicella and MMR.⁵ Therefore, MMR vaccine is a probable triggering factor in their case. We are reporting the second case of AHEI apparently triggered by MMR. AHEI was reported as well after specific infections, including adenovirus,²³ streptococci,²⁴ staphylococci,²⁵ tuberculosis, Coxsackie virus,¹¹ *Campylobacter*,¹¹ rotavirus,²⁶ hepatitis A virus, cytomegalovirus²⁸ and pneumococcal bacteremia.²⁹

REFERENCES

1. Blasini W, Saini R, Vincek V. Acute hemorrhagic edema of infancy: a case report. *Dermatol Online J*. 2007 Jul 13; 13(3):27.
2. Snow IM. Purpura, urticaria and angioneurotic edema of the hands and feet in a nursing baby. *JAMA*. 1913; 61:18-29.
3. Finkelstein H. *Lehrbuch der Sauglingskrankheiten*. 4th ed. Amsterdam: 1938. 814-30.
4. Seidlmayer H. Die Fruhinfantile postinfektiöse Kokarde-Purpura. *Z Kinderheilk*. 1939. 61:217-55.
5. Fiore E, Rizzi M, Simonetti GD, et al. Acute hemorrhagic edema of young children: a concise narrative review. *Eur J Pediatr*. 2011 Dec; 170(12):1507-11.
6. Cunningham BB, Caro WA, Eramo LR. Neonatal acute hemorrhagic edema of childhood: case report and review of the English-language literature. *Pediatr Dermatol*. 1996 Jan-Feb; 13(1):39-44.
7. Yu JE, Mancini AJ, Miller ML. Intussusception in an infant with acute hemorrhagic edema of infancy. *Pediatr Dermatol*. 2007 Jan-Feb; 24(1):61-4.
8. Morrison RR, Saulsbury FT. Acute hemorrhagic edema of infancy associated with pneumococcal bacteremia. *Pediatr Infect Dis J*. 1999 Sep; 18(9):832-3.
9. Carder KR. Hypersensitivity reactions in neonates and infants. *Dermatol Ther*. 2005 Mar-Apr; 18(2):160-75.
10. Fiore E, Rizzi M, Ragazzi M, et al. Acute hemorrhagic edema of young children (cockade purpura and edema): a case series and systematic review. *J Am Acad Dermatol*. 2008 Oct; 59(4):684-95.
11. Legrain V, Lejean S, Taieb A, et al. Infantile acute hemorrhagic edema of the skin: study of ten cases. *J Am Dermatol*; 1991; 24:17-22.
12. Lai-Cheong JE, Banerjee P, Hill V, et al. Bullous acute haemorrhagic oedema of skin in infancy. *Clin Exp Dermatol*. 2007 Jul; 32(4):467-8.
13. Watanabe T, Sato Y. Renal involvement and hypocomplementemia in a patient with acute hemorrhagic edema of infancy. *Pediatr Nephrol*. 2007 Nov; 22(11):1979-81.
14. AlSufyani MA. Acute hemorrhagic edema of infancy: unusual scarring and review of the English language literature. *Int J Dermatol*. 2009 Jun; 48(6):617-22.
15. McDougall CM, Ismail SK, Osmerod A. Acute hemorrhagic oedema of infancy. *Arch Dis Child*. 2005 Mar; 90(3):316.
16. Gattorno M, Picco P, Gambini C, et al. Erythema multiforme-like manifestations and arthritis in a 3-year-old child with leukocytoclastic vasculitis. *Clin Exp Rheumatol*. 1997 May-Jun; 15(3):329-32.
17. Poyrazoglu HM, Per H, Gunduz Z, et al. Acute hemorrhagic edema of infancy. *Pediatr Int*. 2003 Dec; 45(6):697-700.
18. Dubin BA, Bronson DM, Eng AM. Acute hemorrhagic edema of childhood: An unusual variant of leukocytoclastic vasculitis. *J Am Acad Dermatol*. 1990; 23:347-50. PubMed.
19. Garty BZ, Pollak U, Scheuerman O, et al. Acute hemorrhagic edema of infancy associated with herpes simplex type 1 stomatitis. *Pediatr Dermatol*. 2006 Jul-Aug; 23(4):361-4.
20. Millard T, Harris A, MacDonald D. Acute infantile hemorrhagic edema. *J Am Acad Dermatol*. 1999; 41:837-839.
21. Ferreira O, Antunes I, Cruz MJ, et al. Acute hemorrhagic edema of childhood after H1N1 immunization. *Cutan Ocul Toxicol*. 2011 Jun; 30(2):167-9.
22. Obeid M, Haley J, Crews J, et al. Acute hemorrhagic edema of infancy with abdominal pain and elevated transaminases. *Pediatr Dermatol*. 2008 Nov-Dec; 25(6):640-1.
23. Jeannoel P, Fabre M, Payen C, et al. Oedeme aigu hemorrhagique du nourrisson: role de l'adenovirus. A propos d'une observation. *Pediatric*. 1985; 40:557-560.
24. Snoussi N, Strobel M, Heid E, et al. Oedeme aigu hemorrhagique du nourrisson: demonstration d'une vascularite allergique dermique. *Arch Belg Dermatol Syphiligr*. 1973; 29:259-260.
25. Laugier P. Oedeme aigu hemorrhagique (purpura en cocarde avec oedema). *Bull Soc Fr Dermatol Syphiligr*. 1969; 76:462-463.
26. Scocco G. Infantile acute hemorrhagic edema and rotavirus infection. Di Lernia V, Lombardi M, Lo. *Pediatr Dermatol*. 2004 Sep-Oct; 21(5):548-50.
27. Bozaykut A, Atay E, Atay Z, et al. Acute infantile haemorrhagic oedema associated with hepatitis A. *Ann Trop Paediatr*. 2002 Mar; 22(1):59-61.
28. Savino F, Lupica MM, Tarasco V, et al. Acute Hemorrhagic Edema of Infancy: A Troubling Cutaneous Presentation with a Self-Limiting Course. *Pediatr Dermatol*. 2012 Nov 21. doi: 10.1111/pde.12004.
29. Saraclar Y, Tinaztepe K, Adalioglu G, Tuncor A. Acute hemorrhagic edema of infancy (AHEI)-a variant of Henoch-Schönlein purpura or a distinct clinical entity? *J Allergy Clin Immunol*. 1990; 86:473-83.